AMENDMENTS

Please amend the claims following, wherein the deleted matter is shown by strikethrough and the added matter is shown by underlining.

1. (Original) A nanoparticle probe composition for facilitating molecular imaging or monitoring, comprising:

a detectable moiety comprising a magnetic nanoparticle having a biocompatible coating thereon;

a targeting probe attached to the biocompatible coating; and

a delivery ligand attached to the biocompatible coating.

2. (Original) The composition of Claim 1, wherein the targeting probe is a nucleic acid probe.

3. (Original) The composition of Claim 2, wherein the nucleic acid probe hybridizes to a nucleic acid target sequence on a subject nucleic acid and forms a stem-loop structure when not bound to the nucleic acid target sequence.

4. (Original) The composition of Claim 2, wherein the nucleic acid probe comprises a modification of the nucleic acid backbone for the increased stability of the nucleic acid as compared to a naturally occurring nucleic acid.

5. (Original) The composition of Claim 1, wherein the targeting probe is a polypeptide probe.

6. (Original) The composition of Claim 5, wherein the targeting probe is an antibody or fragment thereof.

7. (Original) The composition of Claim 1, wherein the targeting probe is selected from the group consisting of a high affinity ligand, a peptide, and an aptamer.

8. (Original) The composition of Claim 1, wherein the composition comprises two or more targeting probes.

9. (Original) The composition of Claim 1, wherein the delivery ligand comprises a protein transduction peptide selected from the group consisting of HIV-1 TAT, HSV VP22, and ANTP.

10. (Original) The composition of Claim 1, wherein the delivery ligand comprises a peptide selected from the group consisting of W/R, NLS*, AlkCWK18, DiCWK18, transportan, DipaLytic, K16RGD, P1, P2, P3, P3a, P9.3, Plae, Kplae, cKplae, MGP, HA2, LARL46, Hel-11-7, KK, KWK, RWR, and Loligomer.

11. (Original) The composition of Claim 1, wherein the delivery ligand facilitates receptor-mediated endocytosis of the composition.

12. (Original) The composition of Claim 1, wherein the delivery ligand facilitates entry into a cell by permeabilizing the cell membrane.

13. (Original) The composition of Claim 1, wherein the magnetic nanoparticle comprises a metal detectable by use of an MRI instrument that is selected from the group consisting of selected from the group consisting of iron, cobalt, zinc, cadmium, nickel, gadolinium, chromium, copper, manganese, terbium, europium, gold, silver, platinum, and alloys thereof.

14. (Original) The composition of Claim 13, wherein the magnetic nanoparticle is selected from the group consisting of monocrystalline iron oxide nanoparticle (MION), chelate of gadolinium, and superparamagnetic iron oxide (SPIO).

15. (Original) The composition of Claim 13, wherein the magnetic nanoparticle is monocrystalline iron oxide nanoparticle (MION).

16. (Original) The composition of Claim 13, wherein the magnetic nanoparticle is a free metal ion, a metal oxide, a chelate, or an insoluble metal compound.

17. (Original) The composition of Claim 13, wherein the magnetic nanoparticle is selected from the group consisting of Fe_3O_4, Fe_2O_4, Fe_xPt_y, Co_xPt_y, $MnFe_xO_y$, $CoFe_xO_y$, $NiFe_xO_y$, $CuFe_xO_y$, $ZnFe_xO_y$, and $CdFe_xO_y$, wherein x and y vary between 1 and 6, depending on the method of synthesis.

18. (Original) The composition of Claim 13, wherein the magnetic nanoparticle further comprises a metal coating selected from the group consisting of gold, silver, iron, cobalt, zinc, cadmium, nickel, gadolinium, chromium, copper, and manganese, and an alloy thereof.

19. (Original) The composition of Claim 1, wherein the biocompatible coating is selected from the group consisting of a surfactant based coating, a starch based coating, a dextran based coating, a silica based coating, a layer by layer coating, a phospholipid-polyethylene glycol coating, a polymer coating, a mesoporous particle coating, a microporous particle coating, a lipid based coating, and a dendrimer based coating.

20. (Original) The composition of Claim 1, wherein the biocompatible coating is a phospholipid-polyethylene glycol coating.

21. (Original) The composition of Claim 1, wherein the composition further comprises a second delivery ligand that is attached to the biocompatible coating and that interacts with a molecule located on the outer surface of a particular type of cell or tissue.

22. (Original) The composition of Claim 21, wherein the second delivery ligand is selected from a group consisting of an antibody, an antibody fragment, a peptide, an aptamer, a receptor-specific ligand, and a tissue-specific ligand.

23. (Original) The composition of Claim 21, wherein the second delivery ligand that interacts with an infected cell or a diseased cell.

24. (Original) The composition of Claim 1, further comprising a second detectable moiety attached to the biocompatible coating, wherein the second detectable moiety is

selected from the group consisting of resonance energy transfer donor or acceptor moiety; a radioisotope; a fluorescent dye; an organic bead, a chelator, or a magnetic nanoparticle with fluorescent or luminescent characteristics; and an inorganic bead with fluorescent or luminescent characteristics.

25. (Original) The composition of Claim 1, further comprising a therapeutic molecule attached to the biocompatible coating or to the magnetic nanoparticle.

26. (Currently Amended) A composition for facilitating signal transduction in molecular imaging or monitoring, comprising:

a first magnetic nanoparticle probe composition comprising a detectable moiety comprising a magnetic nanoparticle having a biocompatible coating thereon; a first targeting probe attached to the biocompatible coating; and a delivery ligand attached to the biocompatible coating; and

a second magnetic nanoparticle probe composition comprising a detectable moiety comprising a magnetic nanoparticle having a biocompatible coating thereon; a second targeting probe attached to the biocompatible coating; and a delivery ligand attached to the biocompatible coating;

~~wherein the detectable moiety comprises a magnetic nanoparticle having a biocompatible coating thereon;~~ wherein the first targeting probe binds to a first target and the second targeting probe binds with a second target; and wherein an effect on water relaxation from interaction between the first and second magnetic nanoparticles can be detected to determine binding of both the first and the second targeting probes to the first and the second target.

27. (Original) The composition of Claim 26, wherein the first targeting probe and the second targeting probe are nucleic acid probes; wherein the first nucleic acid probe hybridizes to a first nucleic acid target sequence on a subject nucleic acid and the second nucleic acid probe hybridizes with a second nucleic acid target sequence on the subject nucleic acid; and wherein the first nucleic acid target sequence and the second nucleic acid target sequence are separated by a number of nucleotides on the subject nucleic acid such that an effect on water relaxation from interaction between the first and second magnetic nanoparticles can be detected to determine hybridization of both the first and the second nucleic acid probes.

28. (Original) The composition of Claim 27, further comprising

a third magnetic nanoparticle probe composition comprising a detectable moiety comprising a magnetic nanoparticle having a biocompatible coating thereon; a third targeting probe attached to the biocompatible coating; and a delivery ligand attached to the biocompatible coating; and

a fourth magnetic nanoparticle probe composition comprising a detectable moiety comprising a magnetic nanoparticle having a biocompatible coating thereon; a fourth targeting probe attached to the biocompatible coating; and a delivery ligand attached to the biocompatible coating;

wherein the third nucleic acid probe hybridizes to a third nucleic acid target sequence on the subject nucleic acid and the fourth nucleic acid probe hybridizes with a fourth nucleic acid target sequence on the subject nucleic acid; and wherein the third nucleic acid target sequence and the fourth nucleic acid target sequence are separated by a number of nucleotides on the subject nucleic acid such that an effect on water relaxation from interaction between the third and fourth magnetic nanoparticles can be detected to determine hybridization of both the third and the fourth nucleic acid probes.

29. (Original) The composition of Claim 27, wherein the composition further comprises additional magnetic nanoparticle probe pairs.

30. (Currently Amended) The composition of Claim 27, wherein the first nucleic acid probe, the second nucleic acid probe, or both nucleic acid probes hybridize ~~hybridizes~~ to a nucleic acid target sequence on a subject nucleic acid and form ~~forms~~ a stem-loop structure when not bound to the nucleic acid target sequence.

31. (Currently Amended) The composition of Claim 27, wherein the first nucleic acid probe, the second nucleic acid probe, or both nucleic acid probes comprise ~~comprises~~ a modification of the nucleic acid backbone for the increased stability of the nucleic acid as compared to a naturally occurring nucleic acid.

32. (Original) The composition of Claim 26, wherein the first and the second targeting probes are polypeptide probes; wherein the first polypeptide probe binds to a first target sequence on a subject polypeptide and the second polypeptide probe binds with a second target sequence on a subject polypeptide; and wherein the first target sequence and the second target sequence are separated by a distance such that an effect on water relaxation from interaction between the first and second magnetic nanoparticles can be detected to determine binding of both the first and the second polypeptide probes.

33. (Original) The composition of Claim 32, wherein the first and the second target sequences are located on a single subject polypeptide.

34. (Original) The composition of Claim 32, wherein the first target sequence is located on a first subject polypeptide and the second target sequence is located on a second subject polypeptide; and wherein effect on water relaxation from interaction between the first and second magnetic nanoparticles can be detected to determine the interaction of the first subject polypeptide and the second subject polypeptide.

35. (Original) The composition of Claim 32, wherein the first targeting probe, the second targeting probe, or both targeting probes are antibodies or fragments thereof.

36. (Original) The composition of Claim 26, wherein the first targeting probe, the second targeting probe, or both targeting probes are selected from the group consisting of a high affinity ligand, a peptide, and an aptamer.

37. (Original) The composition of Claim 26, wherein the first or the second magnetic nanoparticle probe composition or both comprise two or more targeting probes.

38. (Original) The composition of Claim 26, wherein the delivery ligand comprises a cell penetrating peptide selected from the group consisting of HIV-1 TAT, HSV VP22, and ANTP.

39. (Original) The composition of Claim 26, wherein the delivery ligand comprises a peptide selected from the group consisting of W/R, NLS*, AlkCWK18, DiCWK18, transportan, DipaLytic, K16RGD, P1, P2, P3, P3a, P9.3, Plae, Kplae, cKplae, MGP, HA2, LARL46, Hel-11-7, KK, KWK, RWR, and Loligomer.

40. (Original) The composition of Claim 26, wherein the magnetic nanoparticle comprises a metal detectable by use of an MRI instrument that is selected from the group consisting of selected from the group consisting of iron, cobalt, zinc, cadmium, nickel, gadolinium, chromium, copper, manganese, terbium, europium, gold, silver, platinum, and alloys thereof.

41. (Original) The composition of Claim 40, wherein the magnetic nanoparticle is monocrystalline iron oxide nanoparticle (MION).

42. (Original) The composition of Claim 40, wherein the magnetic nanoparticle is a free metal ion, a metal oxide, a chelate, or an insoluble metal compound.

43. (Currently Amended) The composition of Claim 40, wherein the magnetic nanoparticle is selected from the group consisting of Fe_3O_4, Fe_2O_4, Fe_xPt_y, Co_xPt_y, $MnFe_xO_y$, $CoFe_xO_y$, $NiFe_xO_y$, $CuFe_xO_y$, $ZnFe_xO_y$, and $CdFe_xO_y$, wherein x and y vary between 1 and ~~—~~ 6 depending on the method of synthesis.

44. (Original) The composition of Claim 40, wherein the magnetic nanoparticle further comprises a metal coating selected from the group consisting of gold, silver, iron, cobalt, zinc, cadmium, nickel, gadolinium, chromium, copper, manganese, and an alloy thereof.

45. (Original) The composition of Claim 26, wherein the biocompatible coating is selected from the group consisting of a surfactant based coating, a starch based coating, a dextran based coating, a silica based coating, a layer by layer coating, a phospholipid-polyethylene glycol coating, a polymer coating, a mesoporous particle coating, a microporous particle coating, a lipid based coating, and a dendrimer based coating.

46. (Original) The composition of Claim 26, wherein the biocompatible coating is a phospholipid-polyethylene glycol coating.

47. (Original) The composition of Claim 26, wherein the first magnetic nanoparticle probe composition, the second magnetic nanoparticle probe composition, or both further comprise a second delivery ligand that is attached to the biocompatible coating and that interacts with a molecule located on the outer surface of a particular type of cell or tissue.

48. (Original) The composition of Claim 47, wherein the second delivery ligand is selected from a group consisting of an antibody, an antibody fragment, a peptide, an aptamer, a receptor-specific ligand, and a tissue-specific ligand.

49. (Original) The composition of Claim 47, wherein the second delivery ligand is capable of interacting with an infected cell or a diseased cell.

50. (Original) The composition of Claim 26, wherein the first magnetic nanoparticle probe composition, the second magnetic nanoparticle probe composition, or both further comprise a second detectable moiety attached to the biocompatible coating, wherein the detectable moiety is selected from the group consisting of a resonance energy transfer donor or acceptor moiety, a fluorescent dye, an organic bead with fluorescent or luminescent characteristics, and an inorganic bead with fluorescent or luminescent characteristics.

51. (Original) The composition of Claim 26, wherein the first magnetic nanoparticle probe composition, the second magnetic nanoparticle probe composition, or both further comprise a therapeutic molecule attached to the biocompatible coating or to the magnetic nanoparticle.

52. (Original) A composition for facilitating molecular imaging, comprising two or more magnetic nanoparticle probe compositions within a vesicle, wherein each magnetic nanoparticle probe composition comprises at least one targeting probe and a detectable moiety attached thereto, wherein the detectable moiety comprises a magnetic nanoparticle

having a biocompatible coating thereon, and wherein the vesicle comprises a biocompatible membrane having at least one delivery ligand on its outer surface.

53. (Original) A method of determining expression of a subject nucleic acid, comprising introducing a composition to a sample suspected of expressing the subject nucleic acid; and

detecting the presence of the subject nucleic acid by molecular imaging;

wherein the composition comprises at least one magnetic nanoparticle probe composition comprising a detectable moiety comprising a magnetic nanoparticle having a biocompatible coating thereon; a targeting probe attached to the biocompatible coating that binds to the subject nucleic acid; and a delivery ligand attached to the biocompatible coating.

54. (Original) The method of Claim 53, wherein the composition further comprises a second magnetic nanoparticle probe composition comprising a second nucleic acid probe, a delivery ligand, and a detectable moiety; wherein the second nucleic acid probe hybridizes with a second nucleic acid target sequence on the subject nucleic acid; and wherein an effect on water relaxation from the interaction of the first and second magnetic nanoparticles can be detected to determine the hybridization of the first and second nucleic acid probes to the subject nucleic acid.

55. (Original) The method of Claim 54, wherein the composition is located within a vesicle comprising a biocompatible membrane having a delivery ligand thereon.

56. (Original) The method of Claim 53, wherein the detection of the presence of the subject nucleic acid is measured by magnetic resonance imaging (MRI).

57. (Original) The method of Claim 53, wherein the detection of the presence of the subject nucleic acid is measured by resonance energy transfer signals.

58. (Original) The method of Claim 53, wherein the method is performed *in vivo*.

59. (Original) The method of Claim 53, wherein the sample contains a living cell.

60. (Original) The method of Claim 53, wherein the cell is in a patient.

61. (Original) The method of Claim 60, wherein the composition is introduced by subcutaneous injection, intravenous injection, intradermal injection, intramuscular injection, inhalation, intranasal administration, oral administration, sublingual administration, buccal administration, or topical administration.

62. (Original) The method of Claim 53, wherein the detection of the subject nucleic acid indicates the presence of a virus in the sample, the presence of a cancer in the sample, or an alteration of the expression pattern of the subject nucleic acid in response to an external stimulus.

63. (Original) The method of Claim 53, wherein the delivery ligand comprises a protein transduction peptide selected from the group consisting of HIV-1 TAT, HSV VP22, and ANTP.

64. (Original) The method of Claim 53, wherein the delivery ligand comprises a peptide selected from the group consisting of W/R, NLS*, AlkCWK18, DiCWK18, transportan, DipaLytic, K16RGD, P1, P2, P3, P3a, P9.3, Plae, Kplae, cKplae, MGP, HA2, LARL46, Hel-11-7, KK, KWK, RWR, and Loligomer.

65. (Original) The method of Claim 53, wherein the magnetic nanoparticle comprises a metal detectable by use of an MRI instrument that is selected from the group consisting of selected from the group consisting of iron, cobalt, zinc, cadmium, nickel, gadolinium, chromium, copper, manganese, and an alloy thereof.

66. (Original) The method of Claim 53, wherein the magnetic nanoparticle is monocrystalline iron oxide nanoparticle (MION).

67. (Original) The method of Claim 53, wherein the biocompatible coating is selected from the group consisting of a surfactant based coating, a starch based coating, a dextran

based coating, a silica based coating, a layer by layer coating, a phospholipid-polyethylene glycol coating, a polymer coating, a mesoporous particle coating, a microporous particle coating, a lipid based coating, and a dendrimer based coating.

68. (Original) The method of Claim 53, wherein the biocompatible coating is a phospholipid-polyethylene glycol coating.

69. (Original) The method of Claim 53, wherein the first magnetic nanoparticle probe composition, the second magnetic nanoparticle probe composition, or both further comprise a second delivery ligand attached to the biocompatible coating that interacts with a molecule located on the outer surface of a particular type of cell or tissue, wherein the second ligand is selected from a group consisting of an antibody, an antibody fragment, a peptide, an aptamer, a receptor-specific ligand, and a tissue-specific ligand.

70. (Currently Amended) A method of determining expression of a subject polypeptide, comprising

introducing a composition to a sample suspected of expressing the subject polypeptide; and

detecting the presence of the subject polypeptide by molecular imaging;

wherein the composition comprises at least <u>one</u> ~~two~~ magnetic nanoparticle probe composition comprising a detectable moiety comprising a magnetic nanoparticle having a biocompatible coating thereon; a targeting probe attached to the biocompatible coating that binds to the subject polypeptide; and a delivery ligand attached to the biocompatible coating.

71. (Original) The method of Claim 70, wherein the composition comprises two magnetic nanoparticle probe compositions, wherein the first magnetic nanoparticle probe composition comprises a detectable moiety comprising a magnetic nanoparticle having a biocompatible coating thereon, a first targeting probe attached to the biocompatible coating, and a delivery ligand attached to the biocompatible coating; wherein the second magnetic nanoparticle probe composition comprises a detectable moiety comprising a magnetic nanoparticle having a biocompatible coating thereon, a second targeting probe attached to the biocompatible coating, and a delivery ligand attached to the biocompatible coating; wherein

the first and the second targeting probe bind with a first and a second subject polypeptide; and wherein an effect on water relaxation from the interaction of the first and second magnetic nanoparticles can be detected to determine the interaction of the first subject polypeptide and the second subject polypeptide.

72. (Original) The method of Claim 71, wherein the composition is located within a vesicle comprising a biocompatible coating having a delivery ligand thereon.

73. (Original) The method of Claim 70, wherein the detection of the presence of the subject polypeptide is measured by magnetic resonance imaging (MRI).

74. (Original) The method of Claim 70, wherein the detection of the presence of the subject polypeptide is measured by resonance energy transfer signals.

75. (Original) The method of Claim 70, wherein the method is performed *in vivo*.

76. (Original) The method of Claim 70, wherein the sample contains a living cell.

77. (Original) The method of Claim 70, wherein the cell is in a patient.

78. (Original) The method of Claim 77, wherein the composition is introduced by subcutaneous injection, intravenous injection, intradermal injection, intramuscular injection, inhalation, oral administration, sublingual administration, buccal administration, or topical administration.

79. (Original) The method of Claim 70, wherein the detection of the subject polypeptide indicates the presence of a virus in the sample, the presence of a cancer in the sample, the presence of a disease in the sample, or an alteration of the expression pattern of the subject polypeptide in response to an external stimulus.

80. (Original) The method of Claim 70, wherein the delivery ligand comprises a protein transduction peptide selected from the group consisting of HIV-1 TAT, HSV VP22, and ANTP.

81. (Original) The method of Claim 70, wherein the delivery ligand comprises a peptide selected from the group consisting of W/R, NLS*, AlkCWK18, DiCWK18, transportan, DipaLytic, K16RGD, P1, P2, P3, P3a, P9.3, Plae, Kplae, cKplae, MGP, HA2, LARL46, Hel-11-7, KK, KWK, RWR, and Loligomer.

82. (Original) The method of Claim 70, wherein the magnetic nanoparticle comprises a metal detectable by use of an MRI instrument that is selected from the group consisting of selected from the group consisting of iron, cobalt, zinc, cadmium, nickel, gadolinium, chromium, copper, manganese, and an alloy thereof.

83. (Original) The method of Claim 70, wherein the magnetic nanoparticle is monocrystalline iron oxide nanoparticle (MION).

84. (Original) The method of Claim 70, wherein the biocompatible coating is selected from the group consisting of a surfactant based coating, a starch based coating, a dextran based coating, a silica based coating, a layer by layer coating, a phospholipid-polyethylene glycol coating, a polymer coating, a mesoporous particle coating, a microporous particle coating, a lipid based coating, and a dendrimer based coating.

85. (Original) The method of Claim 70, wherein the biocompatible coating is a phospholipid-polyethylene glycol coating.

86. (Original) The method of Claim 70, wherein the first magnetic nanoparticle probe composition, the second magnetic nanoparticle probe composition, or both further comprise a second ligand that is capable of interacting with a molecule located on the outer surface of a particular type of cell or tissue, wherein the second ligand is selected from a group consisting of an antibody, an antibody fragment, a peptide, an aptamer, a receptor-specific ligand, and a tissue-specific ligand.

87. (Original) A method for producing a magnetic nanoparticle probe composition for facilitating molecular imaging, comprising:

combining a magnetic nanoparticle with a biocompatible coating;

adding a delivery ligand; and

adding a targeting probe.

88. (Original) The method of Claim 87, wherein the delivery ligand comprises a protein transduction peptide selected from the group consisting of HIV-1 TAT, HSV VP22, ANTP, W/R, NLS*, AlkCWK18, DiCWK18, transportan, DipaLytic, K16RGD, P1, P2, P3, P3a, P9.3, Plae, Kplae, cKplae, MGP, HA2, LARL46, Hel-11-7, KK, KWK, RWR, and Loligomer.

89. (Original) The method of Claim 87, wherein the magnetic nanoparticle comprises a metal detectable by an MRI instrument that is selected from the group consisting of selected from the group consisting of iron, cobalt, zinc, cadmium, nickel, gadolinium, chromium, copper, and manganese.

90. (Original) The method of Claim 87, wherein the magnetic nanoparticle is monocrystalline iron oxide nanoparticle (MION).

91. (Original) The method of Claim 87, wherein the biocompatible coating is selected from the group consisting of a surfactant based coating, a starch based coating, a dextran based coating, a silica based coating, a layer by layer coating, a phospholipid-polyethylene glycol coating, a polymer coating, a mesoporous particle coating, a microporous particle coating, a lipid based coating, and a dendrimer based coating.

92. (Original) The method of Claim 87, wherein the biocompatible coating is a phospholipid-polyethylene glycol coating.

93. (Original) The method of Claim 87, further comprising the step of adding a second delivery ligand to the biocompatible coating that is capable of interacting with a molecule

located on the outer surface of a particular type of cell or tissue, wherein the second delivery ligand is selected from a group consisting of an antibody, an antibody fragment, a peptide, an aptamer, a receptor-specific ligand, and a tissue-specific ligand.

94. (Original) The method of Claim 87, further comprising the step of adding a therapeutic molecule to the biocompatible coating.